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GRINDELANE DITERPENOIDS FROM *CHRYSOTHAMNUS NAUSEOSUS*

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Key Word Index—*Chrysothamnus nauseosus*; Compositae; rabbitbrush; structure determination; grindelic acid diterpenoids; 18-hydroxygrindelic acid; ^{13}C NMR.

Abstract—Two new grindelic acid diterpenoids, 18-hydroxygrindelic acid and 18-succinyloxygrindelic acid, were isolated from *Chrysothamnus nauseosus*. The assigned structures rest on their spectroscopic properties as well as chemical interconversions.

INTRODUCTION

As part of a program designed to explore alternative methods of insect control, an examination of xerophytic plants of the sagebrush desert area was undertaken. While several members of this plant community exhibited antifeeding effects on third-instar Colorado potato beetle larvae, an aqueous extract of the aerial parts of *Chrysothamnus nauseosus* (Pall.) Britt (rabbitbrush; Compositae; tribe Astereae) was exceptionally active. We have previously reported the occurrence and antifeeding activity of four new C_{10} polyacetylenes from *C. nauseosus* [1]. These same polyacetylenes were recently reported isolated from *C. viscidiflorus* [2] and may be useful taxonomic indicators at the generic level.

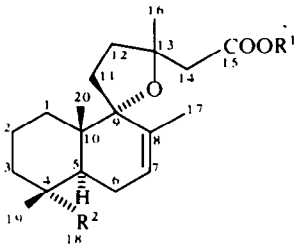
The bicarbonate-soluble portion of the chloroform extracts of *C. nauseosus* also exhibited significant (threshold less than 40 μg/cm^2) antifeeding behavior in third-instar Colorado potato beetle larvae. We report herein isolation and structural elucidation of two new grindelic acid diterpenoids from the bicarbonate-soluble fraction.

RESULTS AND DISCUSSION

Comparison of the ^{1}H NMR spectra of **1** and **3** and their respective methyl esters **2** and **4** suggested a common skeleton differing only in the esterification of the alcohol in **1** by succinic acid. Indeed, treatment of **1** with succinic anhydride followed by methylation with diazomethane yielded a compound indistinguishable from one obtained by treatment of the natural product **3** with diazomethane. Alternatively, hydrolysis of **3** gave a compound indistinguishable from authentic **1**.

Compound **1**, $C_{20}H_{34}O_4$ by high resolution MS, was shown to be a labdane derivative. The ^{1}H NMR spectrum of **1** revealed the presence of two tertiary methyls (δ 0.86), one methyl (δ 1.36) on a carbon also bearing an oxygen and one vinyl methyl (δ 1.75). Assuming **1** to be polyisoprenoid, these data suggested either a normal labdane diterpenoid or a rearranged clerodane diterpenoid skeleton. Both labdane and clerodane diterpenoids have been reported from composites [3, 4]. The mass spectrum of **2** displayed a weak molecular ion at *m/e* 350 and the base peak at *m/e* 210 ($C_{12}H_{18}O_3$) corresponding to a *retro* Diels–Alder rearrangement. This well-documented fragmentation is diagnostic for labd-7-enes and indicated the presence of a double bond at the 7 (8) position [5–7]. Consistent with either a labdane or clerodane skeleton were results obtained from a lanthanide-induced ^{1}H NMR shift study on **2**. Addition of approximately 0.2 molar equivalents of Eu(fod)$_3$ revealed the presence of a one-proton doublet of doublets (J = 11, 4.5 Hz) [8] assignable to H-5 of a labdane system of H-10 of a clerodane system.

Thus far, four of the six C-methyls of the labd-7-ene are accounted for. That C-18 was oxidized to a primary alcohol and that C-15 was oxidized to an acid was supported by the following data. Treatment of **1** with diazomethane yielded methyl ester **2**, the IR spectrum of which displayed absorption (3600, 3450 cm^{-1}) indicating the presence of an alcohol. In addition, the ^{1}H NMR spectrum of **2** contained a two-proton AB quartet centered near δ 3.3 (J = 10.5 Hz) assignable to a hydroxymethylene. Acetylation of the alcohol shifted this AB quartet downfield by 0.45 ppm, the magnitude of which was again supportive of its primary nature. Further support for a hydroxymethylene in **1** was found in a ^{13}C NMR resonance at 72.0 ppm (off-resonance triplet). The ^{1}H NMR chemical shifts of the hydroxymethylene (δ 3.26) and of the acetoxymethylene (δ 3.75) imply an equatorial conformation of these groups [9, 10] and places them at position C-4α. Additional support for the alcohol at C-18 was found by examination of C-methyl ^{1}H NMR chemical shifts [11, 12] upon oxidation of the hydroxymethylene to aldehyde **6** or to acid **7**. If the hydroxymethylene was α at C-4 (and equatorial) then upon oxidation only one C-methyl resonance (C-19) should have been significantly shifted. However, if the hydroxymethylene was β at C-4 (and axial) then upon oxidation both the C-18 and the C-20 methyl resonances should have been shifted. Examination of the ^{1}H NMR spectra of aldehyde **6** and acid **7** revealed that, relative to their chemical shift in the alcohol **2**, only one C-methyl resonance (C-19, $\Delta\delta$ 0.20 and 0.33, respectively) was shifted. Thus, the hydroxymethylene was at C-4α (equatorial). Placement of the alcohol at C-20 in **2**, where again only one ^{1}H NMR C-methyl resonance shift would be expected, is inconsistent with the ^{13}C NMR spectrum



	R^1	R^2
1	H	CH_2OH
2	Me	CH_2OH
3	H	CH_2OCOCH_2COOH
4	Me	CH_2OCOCH_2COOMe
5	Me	CH_2OCOMe
6	Me	CHO
7	Me	COOH
8	Me	COOMe

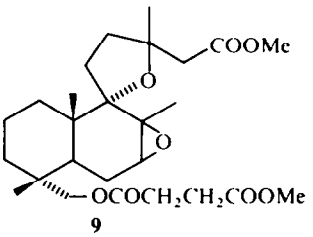


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Table 1. ^{13}C NMR spectral data for compounds **1**–**5** and **7**–**9**[a]

C	**1**	**2**[b]	**3**[c]	**4**[d]	**4**[e]	**5**[f]	**7**[g]	**8**[h,i]	**9**[h,j]
C-1	39.2	38.1	39.0	38.0	38.8	38.4	38.2	38.4	37.7
C-2	18.0	18.0	18.0	17.5	18.3	18.0	18.2	18.3	18.0
C-3	35.4	35.3	35.7	35.7	36.4	36.1	36.6	36.8	36.1
C-4	37.8	37.6	36.9	36.4	36.9	36.7	46.4	46.7	36.8
C-5	37.0	36.7	36.6	37.2	37.6	37.8	38.2	38.4	37.7
C-6	24.1	24.0	23.9	24.0	24.5	24.4	25.5	25.7	23.5
C-7	127.8	126.0	127.4	125.4	126.1	125.9	125.8	125.7	58.9
C-8	133.6	134.7	133.6	134.6	135.1	135.0	135.0	135.3	61.1
C-9	92.0	90.4	92.2	89.8	90.3	90.3	90.6	90.3	88.2
C-10	40.5	40.3	40.5	40.1	40.6	40.5	40.2	40.4	39.7
C-11	34.5[k]	32.4[k]	32.2[k]	32.0[k]	32.5[k]	32.4[k]	31.9[k]	28.4	33.2
C-12	27.7[k]	28.3[k]	28.1[k]	27.9[k]	28.5[k]	28.3[k]	28.5[k]	32.0	31.6
C-13	81.3	80.5	81.9	81.2	81.7	81.6	82.1	81.2	81.5
C-14	47.6	47.8	47.6	47.4	48.1	47.9	47.6	48.0	47.1
C-15	173.0	171.6	172.0[l]	171.6[l]	171.4[l]	171.7[l]	171.8	171.8	172.0
C-16	27.0[m]	27.2[m]	27.0[m]	27.0[m]	27.6[m]	27.4[m]	27.4[m]	27.4	26.9
C-17	21.2[m]	21.1[m]	21.2[m]	20.9[m]	21.4[m]	21.0[m]	21.2[m]	21.3[m]	23.1
C-18	72.0	71.9	72.0	72.9	72.9	73.4	183.5	178.9	73.8
C-19	17.8	17.9	17.9	17.5	18.0	18.0	17.1	17.5	17.6
C-20	17.2	17.1	17.2	16.8	17.3	17.2	17.0	17.1	17.1

[a]The values were recorded at 25.03 MHz and are in ppm downfield from TMS in $CDCl_3$ solution.
[b]Methyl ester carbon at 51.2 ppm.
[c]Succinate carbons at 176.5, 29.2, 29.6 and 174.4 ppm.
[d]Succinate carbons at 172.2, 29.0, 28.6 and 171.2 ppm. Methyl ester carbons at 50.9 and 51.3 ppm.
[e]Spectrum in benzene-d_6. Succinate carbons at 172.1, 29.1, 29.4 and 171.1 ppm. Methyl ester carbons at 50.9 and 51.2 ppm.
[f]Acetoxy carbons at 171.1 and 21.3 ppm. Methyl ester carbon at 51.3 ppm.
[g]Methyl ester carbon at 51.4 ppm.
[h]Assignments may be interchanged, no off-resonance spectrum. [i]Methyl ester carbons at 51.4 and 51.9 ppm.
[j]Other signals at 172.8, 172.0, 51.8, 51.4, 29.4 and 29.0 ppm.
[k,l,m]Values within a column may be interchanged.

which showed two high-field (17.1 and 17.9 ppm), and therefore axial, methyl resonances [13].

The placement of the acid group (IR 1720 cm^{-1}, ^{13}C NMR 173.0 ppm) at C-15 in **1** followed from the absence in the ^1H NMR spectrum of a doublet or triplet C-methyl required of a C-15 methyl and from the presence of an isolated two-proton AB quartet centered near δ 2.62. This AB quartet was consistent with an isolated methylene (C-14) adjacent to a carbonyl and to a fully substituted carbon.

The data so far presented accounted for four of the five sites of unsaturation and three of the four oxygen atoms in **1**. The remaining oxygen atom and site of unsaturation were identified as a cyclic ether by the following information. Treatment of hydroxy ester **2** with acetic anhydride yielded a monoacetate **5** which lacked IR bands assignable to hydroxyl stretching thereby eliminating the presence of a tertiary alcohol. The cyclic ether was implied by two ^{13}C NMR off-resonance singlets (81.3 and 92.0 ppm) assignable to tertiary carbons bearing oxygen. The exceptionally low-field resonance (92.0 ppm) of one of these signals requires that it be adjacent to a quaternary center. This indicated that **1** contained a C-9, C-13 oxygen bridge. Thus **1** belonged to the grindelane-type diterpenes and was 18-hydroxygrindelic acid.

The ^{13}C chemical shifts for **1**–**5** and **7**–**9** are collated in Table 1. Carbon chemical shifts were assigned by a combination of techniques involving comparison with published diterpenoid spectra [14, 15], single frequency off-resonance decoupled multiplicity determinations and chemical shift theory considerations [13]. The high-field shift of C-5 in the herein reported compounds results from a combination of an endocyclic homoallylic effect of the Δ^7-double bond [15–17], a γ (axial)-shielding effect of the ether oxygen [18] and to a lesser extent from a γ-shielding effect of the C-18 hydroxyl [13]. In labdane diterpenoids which lack oxygen at C-9, the C-20 methyl is expected to resonate near 15 ppm [15]. X-ray spectroscopy revealed the α-orientation of the C-9, C-13 oxygen bridge in methyl grindelate [19]. The large negative rotation of methyl grindelate and of the present compounds indicated that they possess the same relative sterochemistry at C-5, C-9, C-10 and C-13. In this configuration, the oxygen is γ and antiperiplanar to the C-20 methyl. Antiperiplanar γ-effects transmitted via quaternary carbons are deshielding (1–5 ppm) [18], hence C-20 in the present compounds would be expected to resonate downfield from its expected 15 ppm value; C-20 is accordingly assigned the highest field off-resonance quartet centered near 17 ppm.

Grindelic acids have now been found in three members of the Astereae tribe, *C. nauseosus* and *Grindelia robusta* [20–22] and *G. squarrosa* [5]. Grindelane diterpenoids occur in another member of the Astereae tribe, *Solidago canadensis* [7] as well as in the family Labiatae [10, 23].

EXPERIMENTAL

Isolation of **1** *and* **3**. *Chrysothamnus nauseosus*, collected 6 October 1978 in the sagebrush desert near Yakima. Washington, was extracted as previously described [1] to yield a $CHCl_3$-partition oil (5.7%, of dry plant). This oil (24.7 g) was extracted with aq. $NaHCO_3$ to yield, after acidification (pH 1), extraction into Et_2O and removal of solvent, a resin (7.20 g, 1.67% of dry plant). CC (Si gel, $CHCl_3$ to 10% MeOH–$CHCl_3$) of this resin yielded two major fractions, A (1.17 g) and B (2.63 g) eluted in that order. Chromatography of fraction A on Amberlyst XN1005 (Ag^+ form), eluting with MeOH, yielded slightly retained (1.1–1.5 void vols) and moderately retained (1.5–2.0 void vols) fractions. The slightly retained fraction (0.36 g) was further purified by HPLC (Si gel, EtOAc, recycle) to yield analytically pure **1** (oil, 0.091 g, 0.02% of dry plant). The moderately retained material (1.69 g) was further separated by Si gel rapid CC [24] (EtOAc–hexanes, 2:1). Semipreparative HPLC (Si gel, $CHCl_3$–MeOH, 96:4, recycle) of the major fraction yielded analytically pure **3** as an oil (0.926 g, 0.2% of dry plant).

18-Hydroxygrindelic acid (**1**). Colorless oil. IR ν_{max}^{neat} cm^{-1}: 3700 2400, 1720, 1390, 1100, 1030, 1000, 760.

	589	578	546	436 nm
$[\alpha]^\lambda$	−82.6	−86.4	−182	−172

c = 1.853 ($CHCl_3$).

^1H NMR (90 MHz, $CDCl_3$): δ 5.57 (*br.*, 1H, $W_{1/2}$ = 7 Hz), 3.39 (*d*, 1H, J = 11 Hz), 3.10 (*d*, 1H, J = 11 Hz), 2.65 (*d*, 1H, J = 15 Hz), 2.59 (*d*, 1H, J = 15 Hz), 1.75 (*br. s*, 3H), 1.36 (*s*, 3H), 0.86 (*s*, 6H); (90 MHz, C_6D_6): δ 5.39 (*br*, 1H, $W_{1/2}$ = 9 Hz), 3.15 (*d*, 1H, J = 1 Hz), 3.00 (*d*, 1H, J = 11 Hz), 2.58 (*d*, 1H, J = 15 Hz), 2.55 (*d*, 1H, J = 15 Hz), 1.62 (*br. s*, 3H), 1.28 (*s*, 3H), 0.77 (*s*, 3H), 0.73 (*s*, 3H); MS (probe) *m/e* (rel. int.): M^+ 336 (0.5), 268 (2), 196 (100), 109 (10); CI-MS (probe) *m/e* (rel. int.): (M + 1) 337 (5), 319 (20), 307 (40), 301 (20), 196 (100), 109 (30); high resolution MS *m/e* 336.2303 (calc. for $C_{20}H_{32}O_4$, 336.2300).

Methyl 18-hydroxygrindelate (**2**). Colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3450, 1725, 1440, 1100, 1060, 1040, 1000, 880.

	589	578	546	436	365
$[\alpha]^\lambda$	−104	−108	−123	−216	−354

c = 0.5925 ($CHCl_3$).

^1H NMR (90 MHz, $CDCl_3$): δ 5.48 (*br*, 1H, $W_{1/2}$ = 9 Hz), 3.63 (*s*, 3H), 3.35 (*d*, 1H, J = 10.5 Hz), 3.12 (*d*, 1H, J = 10.5 Hz), 2.70 (*d*, 1H, J = 15 Hz), 2.60 (*d*, 1H, J = 15 Hz), 1.75 (*br. s*, 3H), 1.32 (*s*, 3H), 0.87 (*s*, 3H), 0.83 (*s*, 3H); (90 MHz, C_6D_6): δ 5.40 (*br.*, 1H, $W_{1/2}$ = 9 Hz), 3.28 (*s*, 3H), 3.10 (*d*, 1H, J = 10.5 Hz), 2.95 (*d*, 1H, J = 10.5 Hz), 2.74 (*d*, 1H, J = 15 Hz), 2.62 (*d*, 1H, J = 15 Hz), 1.70 (*br. s*, 3H), 1.40 (*s*, 3H), 0.80 (*s*, 6H); MS (probe) *m/e* (rel. int.): M^+ 350 (0.4), 332 (0.2), 319 (0.2), 301 (0.4), 289 (0.4), 277 (0.8), 210 (100), 136 (13), 109 (23); high resolution MS *m/e* 350.2476 (calc. for $C_{21}H_{34}O_4$, 350.2457), *m/e* 210.1264 (calc. for $C_{12}H_{18}O_{31}$, 210.1256).

18-Succinyloxygrindelic acid (**3**). Colorless oil; IR ν_{max}^{neat} cm^{-1}: 3650–2400, 1735, 1715, 1390, 1245, 1180, 1000, 770.

	589	578	546	436	365
$[\alpha]^\lambda$	−55	−57	−65	−113	−181

c = 0.663 ($CHCl_3$).

^1H NMR (90 MHz, $CDCl_3$): δ 5.53 (*br.*, 1H, $W_{1/2}$ = 8 Hz), 3.91 (*d*, 1H, J = 11 Hz), 3.57 (*d*, 1H, J = 11 Hz), 2.72 (*d*, 1H, J = 15 Hz), 2.61 (*d*, 1H, J = 15 Hz), 2.60 (*s*, 3H), 1.73 (*br. s*, 3H), 1.40 (*s*, 3H), 0.87 (*s*, 3H), 0.83 (*s*, 3H); MS (probe) *m/e* (rel. int.): M^- 436 (0.9), 418 (0.7), 318 (1), 303 (1), 196 (100), 109 (17), 82 (11); high resolution MS *m/e* 436.2462 (calc. for $C_{24}H_{36}O_7$, 436.2460), *m/e* 196.1093 (calc. for $C_{11}H_{16}O_3$, 196.1099), *m/e* 109.1021 (calc. for C_8H_{13}, 109.1017).

Dimethyl 18-succinyloxygrindelate (**4**). Colorless oil; IR ν_{max}^{neat} cm^{-1}: 1735, 1440, 1260–1230, 1200, 1170, 1100, 1035, 1000.

	589	578	546	436
$[\alpha]^\lambda$	−67.1	−70.1	−80.0	−140.4

c = 1.565 ($CHCl_3$).

^{1}H NMR (90 MHz, $CDCl_3$): δ 5.43 (*br.*, 1H, $W_{1/2}$ = 12 Hz), 3.76 (*d*, 1H, *J* = 11 Hz), 3.69 (*d*, *J* = 11 Hz), 3.64 (*s*, 3H), 3.61 (*s*, 3H), 2.63 (*d*, 1H, *J* = 15 Hz), 2.60 (*s* overlapping *d*, 4H), 1.74 (*br. s*, 3H), 1.31 (*s*, 3H), 0.91 (*s*, 3H), 0.83 (*s*, 3H); (90 MHz, C_6D_6): δ 5.30 (*br.*, 1H, $W_{1/2}$ = 12 Hz), 3.80 (*d*, 1H, *J* = 11 Hz), 3.68 (*d*, 1H, *J* = 11 Hz), 3.31 (*s*, 3H), 3.30 (*s*, 3H), 2.72 (*d*, 1H, *J* = 15 Hz), 2.56 (*d*, 1H, *J* = 15 Hz); 1.38 (*s*, 3H), 0.78 (*s*, 3H), 0.73 (*s*, 3H); MS (probe) *m/e* (rel. int.): M^+ 464 (0.5), 333 (1), 315 (0.7), 301 (0.8), 210 (100), 210 (3), 187 (4), 109 (17); high resolution MS *m/e* 464.2770 (calc. for $C_{26}H_{40}O_7$, 464.2774), *m/e* 210.1258 (calc. for $C_{12}H_{18}O_3$, 210.1256).

Methyl 18-*acetoxygrindelate* (**5**). Colorless oil. IR ν_{max}^{neat} cm^{-1}: 1735, 1420, 1390, 1250, 1100, 1040, 1000, 880.

$[\alpha]^\lambda$	589	578	546	436	365
	−78	−81	−93	−163	−268

c = 0.9705 ($CHCl_3$).

^{1}H NMR (90 MHz, $CDCl_3$): δ 5.45 (*br.*, 1H, $W_{1/2}$ = 7.5 Hz), 3.75 (*br. s*, 2H), 3.63 (*s*, 3H), 2.66 (*d*, 1H, *J* = 15 Hz), 2.62 (*d*, 1H, *J* = 15 Hz), 2.02 (*s*, 3H), 1.75 (*br. s*, 3H), 1.31 (*s*, 3H), 0.92 (*s*, 3H), 0.83 (*s*, 3H); (90 MHz, C_6D_6): δ 5.30 (*br.*, 1H, $W_{1/2}$ = 8.2 Hz), 3.78 (*d*, 1H, *J* = 10.5 Hz), 3.68 (*d*, 1H, *J* = 10.5 Hz), 3.33 (*s*, 3H), 2.67 (*d*, 1H, *J* = 15 Hz), 2.60 (*d*, 1H, *J* = 15 Hz), 1.69 (*s* overlapping *m*), 1.35 (*s*, 3H), 0.81 (*s*, 3H), 0.75 (*s*, 3H); MS (probe) *m/e* (rel. int.): M^- 392 (0.9), 319 (1.2), 304 (0.4), 310 (1), 226 (3), 225 (1), 224 (2), 210 (100), 197 (2), 136 (10), 109 (23).

Methyl 4α-*formylgrindelate* (**6**). A soln of **4** (0.0386 g, 0.083 mM) in MeOH (2 ml) and aq. KOH (1 M, 0.27 ml) was refluxed under N_2 for 5 hr. The reaction mixture was poured into iced H_2O (10 ml) and the mixture extracted with CH_2Cl_2. The separated aq. phase was acidified (conc H_3PO_4, pH 1) then extracted with Et_2O. The Et_2O phase was sequentially extracted with H_2O, with brine, dried ($MgSO_4$), filtered then concd to an oil (0.0314 g). The oil was dissolved in Me_2CO (10 ml), cooled in an ice/water bath (0°) and Jones reagent (2.67 M, 0.035 ml) added to the magnetically stirred soln. The reaction was stirred for 2 hr, quenched with IPA and the salts removed by filtration through a Celite pad. The mother liquor was concd to an oil then partitioned between Et_2O and H_2O. The separated organic phase was sequentially extracted with H_2O, with brine, dried ($MgSO_4$), filtered then concd to an oil (0.0248 g). The oil was dissolved in Et_2O, cooled (0°) and excess CH_2N_2 in Et_2O added. Removal of the solvent gave an oil which was subjected to HPLC (Si gel, hexane–EtOAc, 3:1) to yield pure **6** (colorless oil, 20.1 mg, 69% from **4**). IR ν_{max}^{neat} cm^{-1}: 2675, 1735, 1725, 1450, 1110, 1040, 1020, 1010; ^{1}H NMR (90 MHz, $CDCl_3$): δ 9.27 (*s*, 1H), 5.40 (*br.*, 1H, $W_{1/2}$ = 9 Hz), 3.62 (*s*, 3H), 2.72 (1H, *d*, *J* = 15 Hz), 2.58 (1H, *d*, *J* = 15 Hz), 1.75 (*d*, 3H, *J* = 1.5 Hz), 1.34 (*s*, 3H), 1.09 (*s*, 3H), 0.85 (*s*, 3H).

Methyl 4α-*carboxygrindelate* (**7**). A soln of **4** (0.0557 g, 0.12 mM) in MeOH (3 ml) and aq. KOH (1.07 M, 0.36 ml) was refluxed under N_2 for 4 hr. The cooled reaction mixture was diluted with H_2O then extracted with Et_2O. The separated aq. phase was acidified (conc H_3PO_4, pH 1) then extracted with Et_2O. The separated Et_2O phase was successively washed with H_2O (2 ×), washed with brine, dried ($MgSO_4$) and filtered. To the resulting colorless Et_2O soln at 0° was added an excess of ethereal CH_2N_2. Removal of the solvent yielded an oil which was dissolved in Me_2O (5 ml), cooled to 0° and Jones reagent (2.67 M, 0.044 ml) added. The magnetically stirred reaction mixture was warmed to room temp. and additional Jones reagent (0.045 ml) added and stirring continued for 1.5 hr. The reaction was quenched by the addition of IPA (0.5 ml). The salts were removed by filtration through a Celite pad and the resulting mother liquor concd to an oil. This oil was dissolved in Et_2O and sequentially washed with H_2O (3 ×), washed with brine, dried ($MgSO_4$), filtered then concd to a white solid. Recrystallization (hexane) gave white crystals of **7** (40.1 mg, 91% from **4**), mp 175–177°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–2300, 1725, 1695, 1440, 1385, 1320, 1290, 1230 *br.*, 1100, 1030, 1010, 1000, 895.

$[\alpha]^\lambda$	589	578	546	436	365
	−78	−82	−93	−161	−244

c = 0.614 ($CHCl_3$).

^{1}H NMR (90 MHz, $CDCl_3$): δ 5.42 (*br*, 1H, $W_{1/2}$ = 7.9 Hz), 3.64 (*s* 3H) 2.74 (*d*, 1H, *J* = 15 Hz), 2.66 (*d*, 1H, *J* = 15 Hz), 1.75 (*br. s*, 3H), 1.33 (*s*, 3H), 1.20 (*s*, 3H), 0.83 (*s*, 3H); (90 MHz, C_6D_6): δ 5.29 (*br.*, 1H, $W_{1/2}$ = 8.2 Hz), 3.29 (*br. s*, 3H), 2.75 (*br. s*, 2H), 1.68 (*br. s*, 3H), 1.35 (*s*, 3H), 1.22 (*s*, 3H), 0.70 (*s*, 3H). MS (probe) *m/e* (rel. int.): M^+ 364 (0.7), 332 (0.3), 291 (1.4), 287 (1), 210 (100), 136 (10), 109 (14); high resolution MS *m/e* 364.2251 (calc. for $C_{21}H_{32}O_5$, 364.2249).

Methyl 4α-*carbomethoxygrindelate* (**8**). Colorless oil, IR ν_{max}^{neat} cm^{-1}: 1720, 1440, 1260, 1230, 1100, 1000, 890 (w).

$[\alpha]^\lambda$	589	578	546	436	365
	−63	−66	−76	−132	−198

^{1}H NMR (90 MHz, $CDCl_3$): δ 5.42 (*br.*, 1H, $W_{1/2}$ = 9 Hz), 3.64 (*s*, 3H), 3.62 (*s*, 3H), 2.72 (*d*, 1H, *J* = 15 Hz), 2.61 (*d*, 1H, *J* = 15 Hz), 1.74 (*d*, 3H, *J* = 1.5 Hz), 1.32 (*s*, 3H), 1.21 (*s*, 3H), 0.82 (*s*, 3H); (90 MHz, C_6D_6): δ 5.30 (*br.*, 1H, $W_{1/2}$ = 9 Hz), 3.28 (*s*, 3H), 3.23 (*s*, 3H), 2.68 (*d*, 1H, *J* = 15 Hz), 2.61 (*d*, 1H, *J* = 15 Hz), 1.66 (*br.*, 3H), 1.35 (*s*, 3H), 1.29 (*s*, 3H), 0.74 (*s*, 3H); MS (probe) *m/e* (rel. int.): M^+ 378 (0.6), 319 (0.7), 305 (1), 210 (100), 207 (93), 169 (22), 109 (24); CI-MS (probe) *m/e* (rel. int.): $M^+ + 1$ 379 (40), 361 (54), 210 (100), 207 (93), 169 (22), 109 (24); high resolution MS *m/e* 378.2432 (calc. for $C_{22}H_{34}O_5$, 378.2406).

Epoxidation of **4**. To a cold (0°), stirred soln of **4** (0.199 g, 0.0429 mM) in CH_2Cl_2 (0.5 ml) was added *m*-chloroperbenzoic acid (0.0088 g, 85% pure, *ca* 0.0437 mM) in one portion. The reaction was stirred for 2 hr then allowed to warm to room temp. and stirred for an additional 0.5 hr. The reaction mixture was poured into Et_2O and dilute aq. K_2CO_3. The separated Et_2O phase was sequentially washed with H_2O (2 ×), washed with brine, dried ($MgSO_4$) filtered and concd to a colorless oil (0.0157 g). Chromatography (HPLC, Si gel, hexane–EtOAc, 1:1) yielded, in addition to unreacted **4**, oily **9** as the major product (0.0114 g; 0.0238 mM, 55%). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730, 1450, 1240, 1220, 1170, 1110, 1040.

$[\alpha]^\lambda$	589	578	546	436	365
	−44	−46	−53	−89	−138

c = 0.569 ($CHCl_3$).

^{1}H NMR (90 HMz, $CDCl_3$): δ 3.78 *s*, 2H), 3.68 (*s*, 3H), 3.65 (*s*, 3H), 2.95 (*m*, 1H), 2.73 (*s*, 2H), 2.63 (*s*, 3H), 1.38 (*s*, 3H), 1.31 (*s*, 3H), 0.90 (*s*, 3H), 0.85 (*s*, 3H); MS (probe) *m/e* (rel. int.): M^+ 480 (16), 465 (6), 449 (13), 191 (11), 184 (12), 157 (12), 149 (12), 135 (10), 123 (16), 115 (28), 109 (20), 107 (11).

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